

Nongonococcal Urithritis

BY

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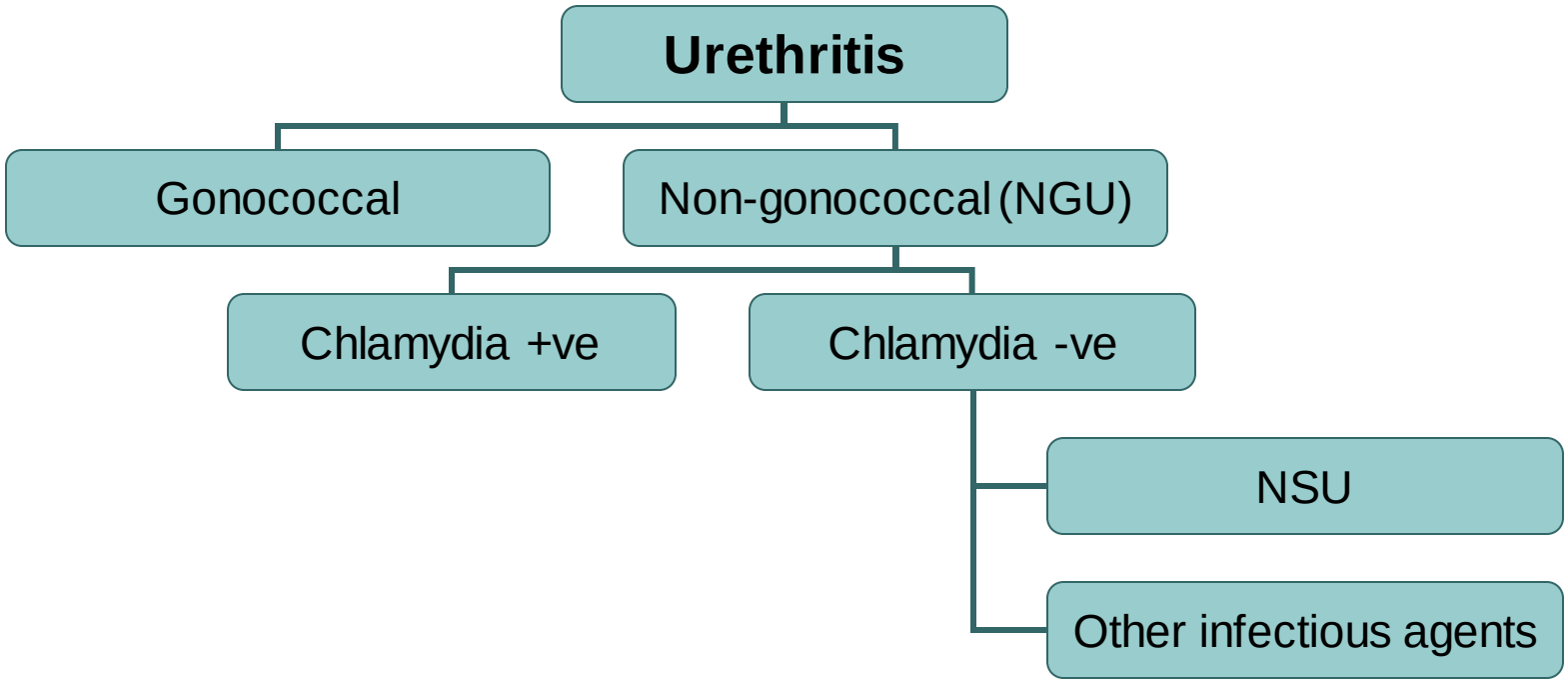
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Introduction

- *Urethritis* means inflammation of urethra. It can be classified into gonococcal and non-gonococcal (NGU). In some cases of NGU, no cause can be detected and are often called “non-specific urethritis.”
- In recent years, the incidence of NGU has increased while that of gonorrhoea has sharply decreased. Compared with gonorrhoea NGU is more frequent in the higher socioeconomic class and is less common in homosexuals.


Urethritis
Gonococcal
Non-gonococcal (NGU)
Chlamydia +ve
Chlamydia -ve
NSU
Other infectious agents

Etiology of NGU

Sexually transmitted microbial agents

Non sexually acquired urithritis

I. Sexually Transmitted Microbial Agents

a) Specific Causes (75%)

1- **Bacteria**

i) Chlamydia Trachomatia (main cause): 30-50% of cases of NGU. Also isolated from 10% of men without urethritis, 15-35% of cases of Gon Urethritis and in 60% of cases of PGU.

ii) Ureaplasma urealyticum 10-40%

iii) Others. e.g. Mycoplasma geitalium, corymebacterium genitalium, Treponema pallidum.

2- **Viruses**

Herpes simplex virus may be the cause in less than 1%. It clears as herpes clears.

3- **Fungi**

Candida (maybe associated with Can-balenrritis, exclude DM).

4- **Protozoa**

Trichomonas Vaginalis (account for over 10% of cases in tropical areas) rapid responses to metronidazole.

II Non-sexually Acquired Urethritis

a) Bacterial urinary tract infections associated with urethritis.
b) Urogenital TB with urethritis.
c) Acute Haemorrhagic cystitis.
d) Stevens-Johnson syndrome.
e) Secondary to: urethral instrumentation, urithral stricture, renal stones, phosphaturia.

Biology of Chlamydia

1- Although they simulate viruses in being **obligatory intracellular parasites**, however they are considered **bacteria** due to:

a) Have cell wall similar to that of gram -ve bacteria.

b) Contain both DNA and RNA.

c) Multiply by binary fission.

d) Sensitive to the antibiotics e.g. Azithromycin, tetracycline, erythromycin and sulphonamides.

2- They cannot grow on artificial media but grow on yolk sac and chick embryo (as virus).

3- There are 4 species of chlamydia

a) **C. trachomatis**: produces glycogen-containing inclusion bodies that stain with iodine and are sensitive to sulphonamides.

b) **C. Psittaci**: glycogen –ve IBs and resist sulphonamides.

c) **C. pneumoniae**: reasonable for respitory dis- Glycogin –ve IB.

d) **C. pecorum**: cause pneumonia and diarhoea in cattles.

4- All chlamydiae have a common group antigen = a lipoplysaccharide complex. By micro- IF test, 15 serotypes have been differentiated for C. trachomatis:

a) Serotypes A,B,Bl,C: Trachoma of eye.

b) Serotypes D,E,F,G,H,I,J,K:

- inclusion conjunctivitis.
- NGU, epididymitis, proctits, cervicitis and salpingitis.
- Neonatal pneumonia.

c) Serotypes L_1, L_2, L_3 : Lymphog.venereum (LGV)

5- C. trachomatis strains → Infect mucous membranes especially columnar, with exception of LGV → Lymphatics.

6- **Life cycle**: they have two developmental forms:

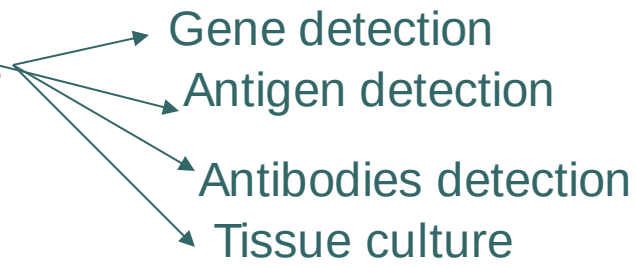
a) **Elimentary body**: infectiuos form, adapted to extracellular survival.

b) **Initial body** (inclusion body, or reticulate body): non-infective, intracellular, metabolicaly active replicating form.

The elementary body attaches itself to the surface of a susceptible cell and they enter the cell. Inside the cell it becomes an initial body which divides by binary fission, then reorganize and condenses into elementary bodies which are released after rupture of host cell, to infect other cells.

7- Although chlamydia infections produce abundant immune response, the latter neither enhances nor protect against infection.

8- **Diagnosis**



a) **Gene Detection by polymerase chain reaction (PCR):** the specimen taken is urine. It is non-invasive, sensitive and specific test. It is a good screening test especially in asymptomatic patients.

b) **Antigen Detection Tests**

i) **Enzyme linked imunosorbent assay (ELISA):** it depends on the detection of chlamydia antigen in the sample by absorbing it to polystyrene beads coupled to chlamydia monoclonal antibodies detected by spectrophotometer.

ii) **Immunofluorescence test (Micro Trak Test):** detects chlamydia conjugated with fluorescein. These tests are sensitive, specific and good for screening, but not recommended for follow up after treatment as the antigen may persist despite death of the organism.

c) **Antichlamydial antibodies detection:** by microimmunoflurescence or complement fixation. These tests are significant only with a rising titre of IgG (4 times rise).

d) **Tissue Culture:** scrapping the urethra or swabing the cervix is done to obtain specimens containing epithelial cells as chlamydia are obligate intracellular organisms. Inoculation into tissue culture is done and chlamydia grows inside the cytoplasm of formed giant cells. Culture is examined 48 hours, with iodine or immunofluorescence → Intracellular chlamydia inclusion bodies. Although tissue culture is expensive and scrapping is invasive technique, it is a sure diagnostic test and can be used to detect antibiotic sensitivity of chlamydia and to examine effect of therapy as they turn -ve after effective therapy.

Clinical Features of Chlamydia Infections in Men

- **Urethritis**
 - I.P → 2-3 weeks.
 - Mild urethritis with slight mucoid or mucopurulent discharge, worse in early morning. Male sexual partners of women who carry C. trachomitis in the cervix may also carry the organism in urethra without symptoms (asymptomatic NGU) which should be treated as well.
 - Tendency to recurrences and chronicity.

Diagnosis:

1. Gram-strained urethral smear → PNM + high number of epithelial cells + no organism.
2. Culture → no organism.
3. Turbidity of urine or threads in the first glass of the two glass test . Better after patient has held his urine for some hours or overnight.
4. Identification of chlamydia, U. urealyticum or other organisms (if available).

Prognosis:

1. Rapid response to azithromycin, tetracycline or erythromycin in 80-90% of NGU cases.
2. Recurrences which respond every time to antibiotics.
3. Numerous attacks of NGU with incomplete or short-lived response to antibiotics (10% of cases) → Frequently recurrent or persistent NGU.

If NO response at all: tetracycline-resistant ureaplasm, T. vaginals, abnormalities of urinary tract or urethrophobia should be suspected.

- **Frequently recurrent or persistent NGU:**

NGU recurs within days or weeks (at least 4 episodes a year) after full antibiotic treatment or does not respond completely. These cases account for 10% of NGU cases.

- Etiology:

1. Insufficient antibiotic treatment.
2. Inappropriate antibiotic treatment, e.g. NGU due to tetracycline resistant U. urealyticum which respond to erythromycin.
3. Reinfection.
4. Organism may remain in protected site as prostate.
5. Excess alcohol or sex activity.
6. Psychological factors e.g. anxiety with frequent recurring NGU.

- Postgonococcal urethritis “PGU”:

 After successful treatment of gonorrhoea with penicillin or spectinomycin, 5-50% of cases develop a NGU termed PGU. It is found that C. trachomatis is more frequently with PGU (79%), than with either NGU (50%). The role of U. urealyticum in PGU is of little importance. Patients with PGU have a double infection of gonorrhoea and NGU the later will persist due to longer IP after gonorrhoea have been eliminated. So **it is better to follow penicillin or spectinomycin treatment of gonorrhoea by a course of tetracycline.**

N.B. Urethrophobia: may follow frequent recurrences of NGU. Such patients observe themselves obsessively and squeeze the urethra repeatedly to prove infection.

II Other Features of Genital Chlamydial Infections in Men

1. Prostatitis: dispute claims of active involvement of chalmydia in chronic prostatitis, there is no evidence that chlamydia are implicated directly in the disease.
2. Epididymitis: as a complication of NGU in 1% of cases.
3. Urethral stricture
4. Infertility: chlamydia may infect the testis, but chlamydia as a cause of inferitility is most unlikely.
5. NG proctitits: mainly in passive homosexuals.
6. Reiters syndrome (and sexually acquired reactive arthritis): Reactive arthritis is an aspectic artritis which follows an infection elsewhere in the body. Reiters syndrome a seronegative arthropathy (absence of rheumatoid factor). It is a triad of reactive arthritis, genital tract inflammation and ocular inflammation. Many patients also develop mucocutaneous leisons.

Clinical Features in Women

C. Trachomates is an important sexually transmitted agent which often cause **asymptomatic infection**, and may occur with other sexually acquired agents, in particular N. gonorrhoea.

1. Bartholinits
2. Cervicitis: the cervix is the 1ry target for chlamydia infection. Infection of cervix is often asymptomatic.
3. Cervical intraepithelial neoplasia
4. Decrease pregnancy rate following IVF maybe associated with presence of chlamydial antibodies.
5. Infection in pregnancy may lead to spontaneous abortion, prematurity, still birth, neonatal death or post partum endometritis.

Neonatal Chlamydial Infections

This occurs during labour from infected cervix.

1. Neonatal conjunctivitis: develop 7-14 days after birth and is usually self limiting, but may be persistent with usual disturbance.
2. Infantile pneumonia: develop 4-12 weeks after birth tachypneic infant with characteristic staccato poroxysmal cough.
3. Otitis media.

N.B The occurrence of ophthalmic neonatorum or chlamydial respiratory disease should be considered as a strong indicator of STD in parents.

Biology of mycoplasmas

1. Very small microorganisms 125-250mm in size, belonging to the *class of cell wall free bacteria.*
2. Contain both DNA and RNA. Has no rigid cell wall, but it is bounded by trilamellar plasma membrane rich in cholesterol.
3. Grown on artificial media or cell-free media as agar and it requires sterols for growth.
4. Stain with Gemsa stain.
5. All strains show absolute resistance to penicillin (as they lack the cell wall), but are inhibited by tetracyclin and erythrocin.

6. Four species are of 1ry importance in humans:
 - Ureplasma urealyticum → NGU in men and lung disese in prematrue infants.
 - Mycoplasma genitalium → uretheral and other infections.
 - Mycoplasma pneumaniae → pneumaniae.
 - Mycoplasma homenis → post partum fever.

N.B. U.urealyticum is normal inhbritant of the genital tract of 5-20% of sexually active men and 40-80% of sexually active women.

7. Diagnosis

- Swabs or urine should be held immediately in mycoplasma medium or stawrt medium at 4 degrees Celsius until culturing. Culture also occurs in an atmosphere of N +10% CO_2 at 37 degrees Celsius.
- Color change in medium containing arginin suggests prsence of M.hominis where color changes in medium containing urea suggests U.urealyticum.
- Ureaplasma colonies. Adding lincomycin (active against M.homins only) or Erythromycin (active against U.urealyticum) can differentiate between both media.
- Serological identification is done by immunoflorescence.
- Ureaplasma produce very small colonies (50-100mm in diameter), with characteristic brown color due to its ability to utilize urea.

- Clinical Spectrum

1) **Male:**

- ✓ NGU → M.homonis and U.urealyticum.
- ✓ Epididymitis → U.urealyticum.
- ✓ Prostatitis.
- ✓ Reiters syndrome.

2) **Female:**

- ✓ Inflamatory Pelvic disease → M.homones and U.urealyticum.
- ✓ Post-abortal and postpartum fever M.homones.
- ✓ Spontaneous abortion, prematurity and low birth weight → both.

3) **Infertility:** *Male & Female*

Treatment: **Tetracyline** is drug of choice for urogenital tract infections with U.urealyticum and M.hominis. But if only U.urealyticm is isolated → **Erythormycin** is given.

Treatment of NG infections

NGU and PGU are less responsive to antibiotics then gonorrhoea and unlike gonorrhoea, relapses may occur.

I. **NGU, PGU, NG Cervitis, Proctis, Conjunctritis.**

- **Tetracycline** 500mg 4 times daily or Doxycycline 100mg twice daily for 7 days. Drug of choice whether NGU is due to C.trachomatis, U.urealyticum or no microbial agent can be found. Avoid milk products that inhibit tetracycline activity.
- **Azithromycin** (Zithromycin Cap 250mg): 1gm single dose → high cure rule for both chlamydia and Gonorrhoea.
- During pregnancy: **Erythromycin stearate** 500mg 4 times daily for 7 days.

- 10% of U.urealyticum are resistant to tetracycline but response to erythromycin or even Doxycycline.
- **Oflaxin** 400mg twice daily for 7 days.
- Avoid sexual intercourse, or use condoms and restrict alcohol intake.

II. Neonatal Conjunctivitis:

Erythromycin syrup 50mg/kg daily in 4 divided doses for 2 weeks.

Follow Up

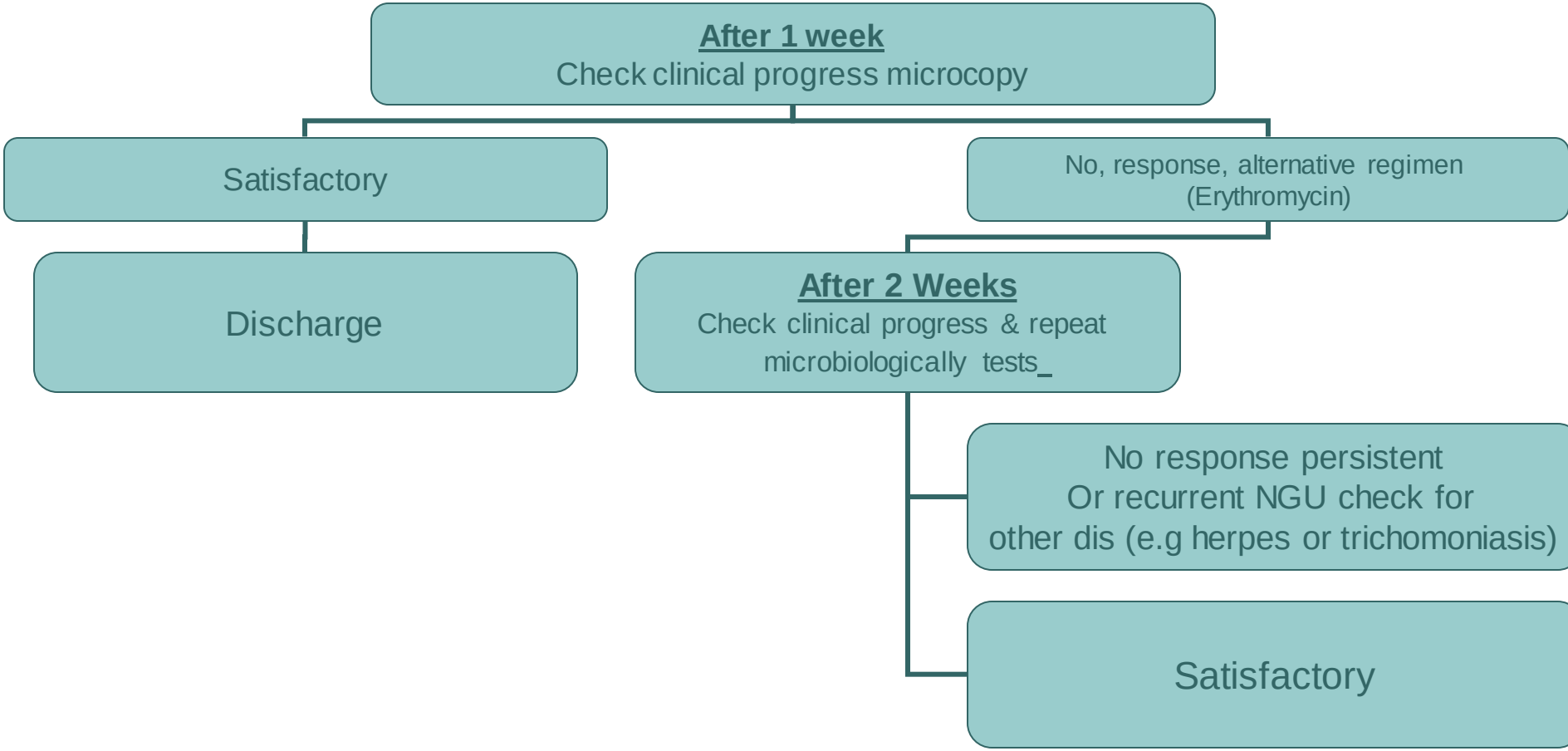
- **1 week after treatment**
 - Asses the efficacy of treatment clinically and microbially.
 - Results of initial tests will be available → confirm or change treatment.
 - Failure to respond to therapy → change treatment → Erythromycin.

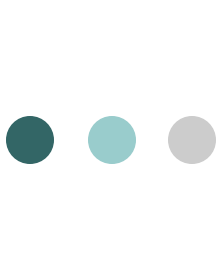
- **2 weeks after completion of treatment**
 - Inadequate response → persistent or recurrent NGU.
- **2-3 weeks after initial visit** → serology of Syphilis.

Advise and Follow Up

avoid sexual intercourse & milk products

investigate & treatment of contacts





Thank You